REMARKS

Claims 25, 31, 33, and 36 are pending. Claims 38-40 have been added. Reconsideration of Claims 25, 31, 33, 36, and 38-40 in view of the above amendments and following remarks is respectfully requested.

Examiner Interview

Applicants note with appreciation the telephonic interview with Examiner Weddington held August 12, 2009. Applicants' attorney, George Renzoni, conferred with Examiner Weddington regarding the appropriateness of the final rejection of claims made in the Office Action dated July 7, 2009. Examiner Weddington agreed that, because all of the claims had not previously been rejected, the final rejection was improper.

A non-final Office Action was mailed August 20, 2009.

The Rejection of Claims 25, 31, and 36 Under 35 U.S.C. § 102(b)

Claims 25, 31, and 36 stand rejected under 35 U.S.C. § 102(b), as anticipated by Freeman et al., *Circulation 103*:357-372, January 2001. Withdrawal of the rejection is requested for the following reasons.

Claim 36 is an independent claim and Claims 25 and 31 depend from Claim 36.

Claim 36 recites a method for enhancing glucose uptake into warm-blooded animal adipocytes comprising administering to a warm-blooded animal in need thereof an effective amount of pravastatin or pharmacologically acceptable salts or esters thereof sufficient to enhance glucose uptake into warm-blooded animal adipocytes, wherein the glucose uptake occurs from the interstitial fluid of peripheral adipose tissues.

Applicants submit that because the Freeman reference does not describe, either expressly or inherently, the claimed invention, the claimed invention is not anticipated by the reference.

More specifically, the Freeman reference fails to describe the claimed method in which glucose uptake into warm-blooded animal adipocytes is enhanced and furthermore that glucose uptake into cells and glucose transport across the endothelium do not share the same mechanisms. Attached herewith is the declaration of Dr. Takagi to support applicants' position that the Freeman reference is not anticipatory.

The Freeman reference describes a retroactive study of human subjects treated with pravastatin to determine whether pravastatin influenced the risk of developing diabetes over time. The study concluded that pravastatin therapy significantly reduced the risk of developing diabetes in the treated group. The authors of the study speculate that three known effects of pravastatin therapy may play a role in the development of diabetes: (1) the lowering of triglycerides, (2) the anti-inflammatory properties of pravastatin, and (3) the effect of pravastatin on endothelial function. See Takagi Declaration, paragraph 3.

The methods described in the above-identified patent application are based on the discovery that an HMG-CoA reductase inhibitor enhances glucose uptake in warm-blooded animal cells, in particular warm-blooded animal adipocytes. The present application describes that the HMG-CoA reductase inhibitor pravastatin enhances glucose uptake into a mouse adipocyte cell line (3T3-L1). The present application further describes increased glucose uptake in adipocytes isolated from mouse strains administered pravastatin. See Takagi Declaration, paragraph 4.

The Freeman reference does not disclose the methods described and claimed in the above-identified patent application. As mentioned above, the Freeman reference merely speculates that three known effects of pravastatin therapy may explain the finding that pravastatin therapy may reduce the propensity of subjects within the study to develop diabetes.

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS PLLC
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

However, none of these three effects is disclosed as being related to glucose uptake by adipocytes. See Takagi Declaration, paragraph 5.

The Freeman reference further states that "there may be other direct or indirect effects of pravastatin therapy on glucose control that have yet to be unraveled." See page 361, left hand column, third full paragraph of the Freeman reference. The present application has identified and demonstrated that pravastatin directly regulates glucose uptake by warm-blooded animal cells, including adipocytes. The work described and claimed in the present application has made a substantial contribution to the field of insulin resistance that may be useful for the treatment of diabetes and related conditions. In contrast, the Freeman reference merely speculates that pravastatin may have other effects on glucose control, without providing any data as to what those effects may be. See Takagi Declaration, paragraph 6.

Applicants respectfully submit that the Freeman reference does not support a conclusion that administration of pravastatin to a warm-blooded animal would necessarily enhance glucose uptake into adipocytes. The Freeman reference suggests that pravastatin may affect numerous unrelated biological processes, any one of which may correlate with for the findings of the Freeman study. However, the Freeman reference does not mention or even speculate that enhanced glucose uptake into adipocytes may account for the decreased risk of diabetes observed in the study. See Takagi Declaration, paragraph 7.

The Patent Office has stated that glucose transport as described in the Freeman reference has the same characteristics as glucose uptake. See the Office Action mailed December 4, 2008. The Freeman reference mentions the effect of pravastatin on endothelial function. See third paragraph at first column on page 361 of the Freeman reference. The Freeman reference speculates that pravastatin restores endothelial function and affects glucose and insulin transport through restoration. However, the reference fails to provide any scientific evidence that supports

this speculation. Therefore, because the Freeman reference does not disclose the function of pravastatin on enhancing glucose transport, the skilled person would not understand the function of pravastatin on enhancing glucose transport based on the Freeman reference. See Takagi Declaration, paragraph 8. Therefore, it cannot be fairly stated that glucose transport as described in the Freeman reference has the same characteristics as glucose uptake. Moreover, for these reasons, it cannot be fairly stated that the Freeman reference describes the claimed method.

In contrast to the Freeman reference and its lack of teaching with regard to the function of pravastatin on enhancing glucose transport, the present application demonstrates that pravastatin directly enhances insulin-induced glucose uptake into warm-blooded animal adipocytes both *in vivo* (see Example 1) and *in vitro* (see Example 2).

As noted above, the Patent Office has stated that glucose transport as described in the Freeman reference has the same characteristics as glucose uptake. Applicants further submit that glucose transport across the endothelium is a different process than insulin-induced glucose uptake into warm-blooded animal cells such as adipocytes. Glucose transport across the endothelium refers generally to movement of glucose from capillaries into tissues. Insulin-induced glucose uptake refers to movement of glucose from the extracellular space into the selective cells in an insulin-dependent manner. Therefore, insulin-induced glucose uptake into cells and glucose transport across the endothelium do not share the same mechanisms of action. See Takagi Declaration, paragraph 8. Because

Because the invention as now claimed is not exactly described by the cited reference, the cited reference is not anticipatory. Withdrawal of the rejection is respectfully requested.

The Rejection of Claims 25, 31, 33, and 36 Under 35 U.S.C. § 103(a)

Claims 25, 31, 33, and 36 stand rejected under 35 U.S.C. § 103(a), as unpatentable over Freeman et al., *Circulation 103*:357-372, January 2001, in view of U.S. Patent No. 5,643,868,

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS PLLC
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

issued to Weiner et al., and further in view of Paolisso et al., *European Journal of Clinical Pharmacology*, Vol. 40, No. 1, pp. 27-31 (1991). Withdrawal of the rejection is requested for the following reasons.

Claim 36 is an independent claim and Claims 25, 31, and 33 depend from Claim 36.

As discussed above with regard to the Section 102 rejection, the Freeman reference does not describe, either expressly or inherently, the claimed invention. More specifically, the Freeman reference fails to teach or suggest the claimed method in which glucose uptake into warm-blooded animal adipocytes is enhanced. Because the cited references fail to teach or suggest every limitation of the claimed method, the claimed method is non-obvious and patentable over the cited references.

The deficiencies of the teaching of the Freeman reference noted above are not cured by the teachings of the Weiner reference and/or the Paolisso reference. The Weiner reference discloses methods for treating a disease in mammals having the characteristics of Type 1 diabetes, where the method includes the step of administering insulin or disease suppressive fragments of insulin or analogs to the mammals. The Paolisso reference discloses that administering simvastatin to non-insulin dependent diabetic patients improves the action of insulin as demonstrated by stronger inhibition of hepatic glucose output and stimulation of both the glucose disappearance rate and the glucose metabolic clearance rate. Neither the Weiner nor the Paolisso reference discloses a method in which glucose uptake into warm-blooded animal adipocytes is enhanced by administration of pravastatin. Therefore, neither the Weiner nor the Paolisso reference cures the deficiency of the Freeman reference.

Because the cited references, either alone or in any combination, fail to teach, suggest, provide any motivation to make, or otherwise render obvious the claimed invention, the claimed

invention is non-obvious and patentable over the cited references. Withdrawal of the rejection is respectfully requested.

New Claims 38-40

Claims 38-40 have been added. Claim 38 is an independent claim similar to Claim 36. Claim 38 recites a method for enhancing insulin-induced glucose uptake into warm-blood animal adipocytes in an insulin-dependent manner. In the method, an effective amount of insulin and pravastatin or pharmacologically acceptable salts or esters thereof sufficient to enhance glucose uptake into warm-blooded animal adipocytes is administered. Claims 39 and 40 depend from Claim 38 and correspond to presently pending Claims 25 and 31. Support for Claims 38-40 can be found throughout the specification as originally filed.

For the reasons set forth above, applicants believe that the invention of Claims 38-40 is novel and non-obvious in view of the cited references.

Conclusion

In view of the above amendment and foregoing remarks, applicants believe that Claims 25, 31, 33, 36, and 38-40 are in condition for allowance. If any issues remain that may be expeditiously addressed in a telephone interview, the Examiner is encouraged to telephone applicants' attorney at 206.695.1755.

Respectfully submitted,

CHRISTENSEN O'CONNOR
JOHNSON KINDNESS[PLLC]

George E. Renzoni

George E. Renzoni, Ph.D.
Registration No. 37,919
Direct Dial No. 206.695.1755

GER:md

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS[PLLC]
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100